

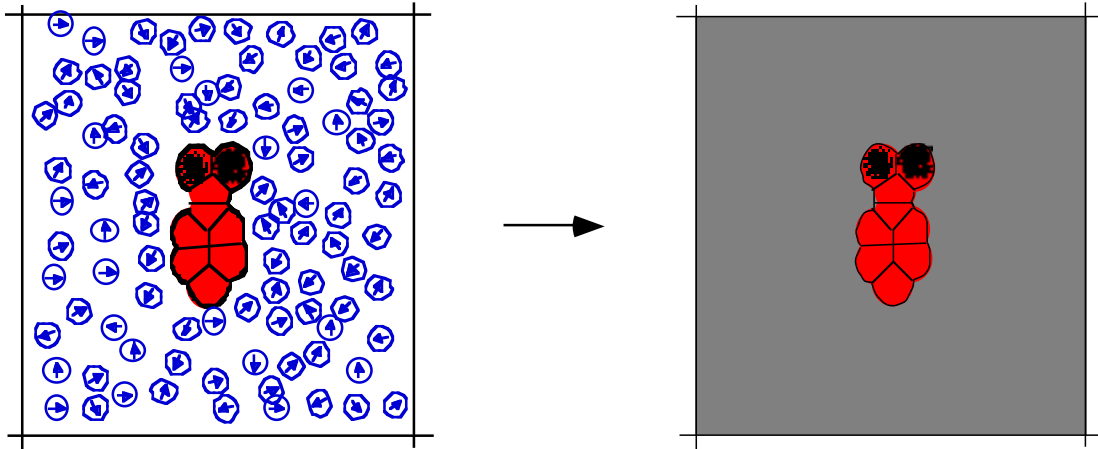
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**“Mixed direct-iterative  
methods for boundary  
integral formulations of  
dielectric solvation  
models,”**

**Corcelli, Kress, Pratt,  
and Tawa**

# dielectric solvation models (i)

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$$\nabla \bullet \boldsymbol{\epsilon}(\mathbf{r}) \nabla \Phi(\mathbf{r}) = -4\pi \rho(\mathbf{r})$$

# dielectric solvation models (ii)

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- \* They couple naturally to electronic structure tools.
- \*  $k_B T$ -level accuracy is often required. This is numerically difficult.
- \* Many coarse accuracy tests are available, but high resolution numerical and physical tests are rare.
- \* Boundary element methods are the 'high accuracy' methods for these applications because the molecular surfaces are complicated.
- \* They are physical, applicable to biomolecules in solution and to ionization equilibria.

# dielectric solvation models (iii)

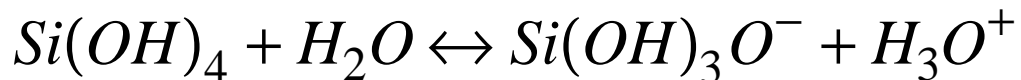
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- \* Testing is also complicated by the fact that these methods are empirical in designation of molecular volumes, surfaces, radii.
- \* Generally these radii must be understood to depend on solution conditions, *i.e.*, temperature, composition, pressure.

# goal of this work

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- \* **test the dielectric solvation model:**
  - » using high accuracy numerical methods.
  - » on a case for which a prior calibration study might be expected to have removed most of the uncertainty in the empirical parameters.
  - » on a case that was not, however, an explicit participant in the prior calibration study:



# numerical methods (i)

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- \* **solvation model: boundary integral formulation for numerical solution of the model macroscopic Poisson equation.**
  - » The algorithm is not identical to prior boundary integral approaches, *e.g.* surface *dipole densities* are used to represent the induced electric potential.
  - » The molecular surface (not Connolly surface) is used and 'good-lattice' techniques are used to tessellate the surface. This permits
    - simple, automated tessellation of the molecular surface,
    - simple studies of numerical convergence with resolution of the surface tessellation,
    - simple transference of detailed, intermediate numerical results between coarse and fine lattices.

# numerical methods (ii)

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## \* solvation model (continued):

- » The approach permits modeling of solute polarizability by assigning an 'interior dielectric constant' for the solute molecule.
- » In the paper are the details of the algorithm.
  - Those details are set to permit a multigrid organization of the numerical work.
  - Practice in the present case was:
    - † first, obtain a direct 'coarse' solution at the highest resolution that was convenient;
    - † second, starting from the coarse solution obtain a 'fine' solution by Gauss-Seidel iteration on a sufficiently higher resolution tessellation of the molecular surface.

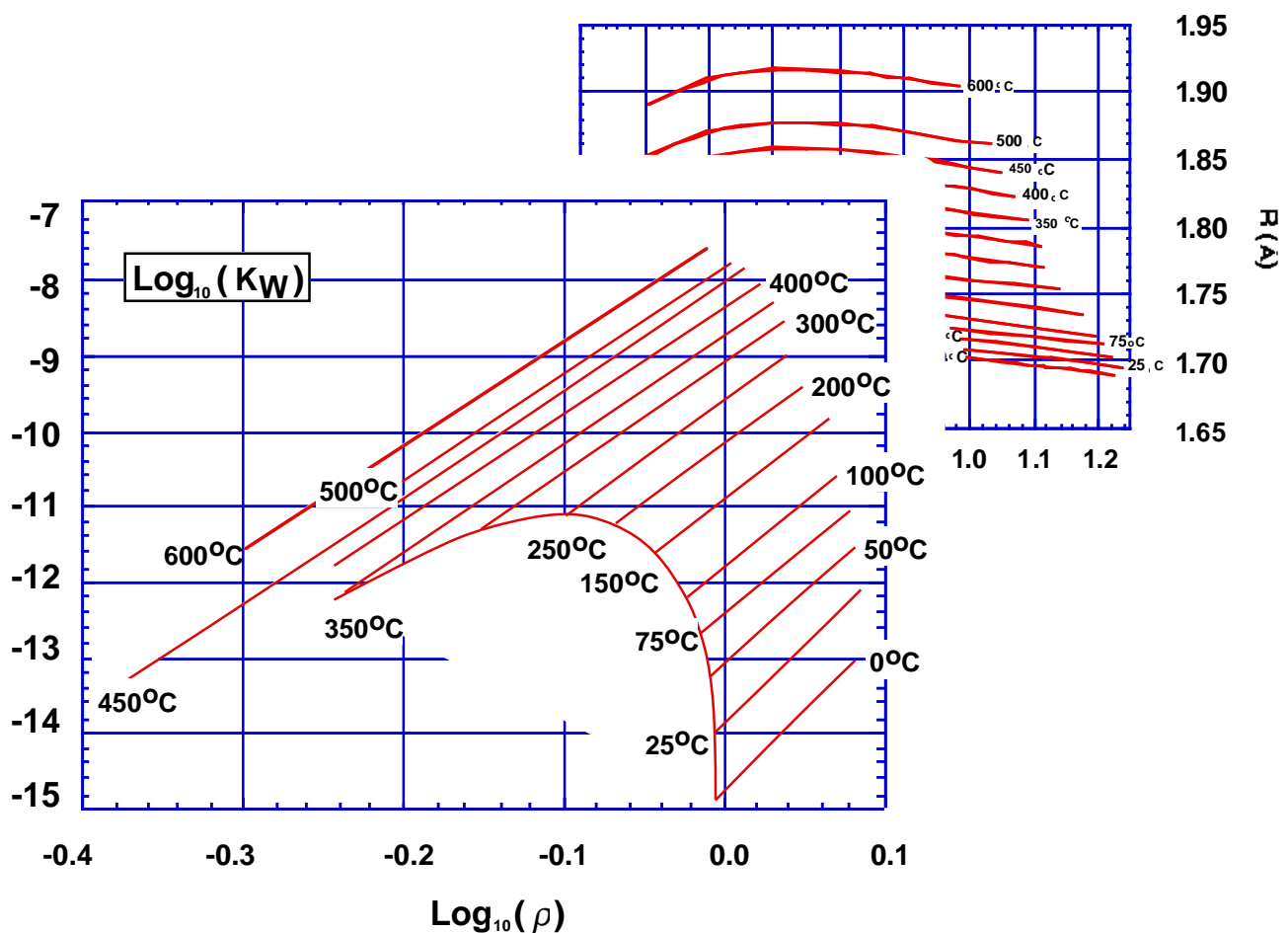
## numerical methods (iii)

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- \* **electronic structure: structures, energies, and polarizabilities of the isolated solute molecules were obtained with GAUSSIAN-92 as detailed in the paper.**



# calibration study (i): pK<sub>w</sub> over a wide range of conditions



## calibration study (ii)

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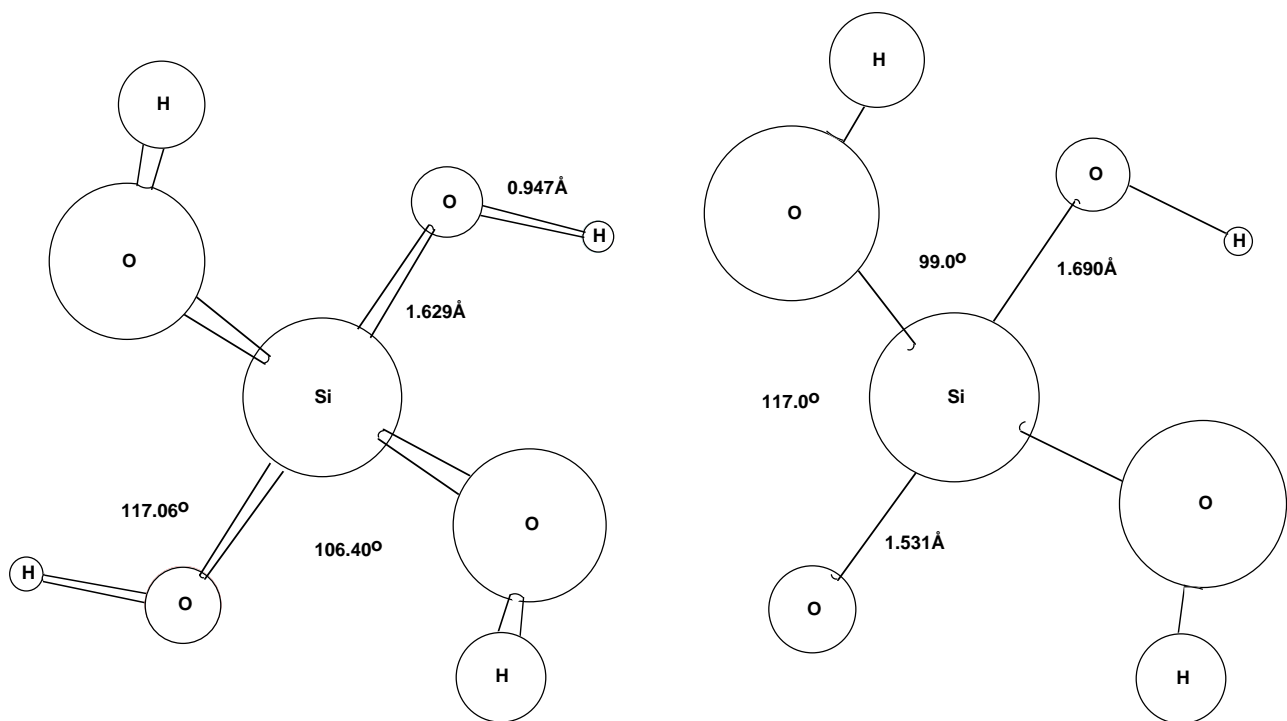
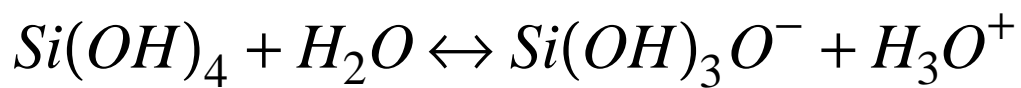
- \* For this equilibrium there is no loss of chemical bonds upon reaction. This is likely the physical case but it is also expected to be simpler for the model not to have to treat physically the ambiguous species “H<sup>+</sup>.”
- \* Reactants and products were assigned a detailed and realistic isolated molecule partial charges based upon electronic structure results.
- \* Reactants and products were assigned a polarizability based upon the known polarizability of H<sub>2</sub>O;  $\epsilon_m = 2.42$ .

## calibration study (iii)

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- \* Reactants and products were assumed to have spherical shape with radius  $R$ , adjusted to match the known experimental values of  $pK_w$ . This is the calibration for ionization of hydroxy-acids.
- \* It was possible to get a perfect fit of calculation to experiment with adjustment of  $R$ .
- \* It was necessary that  $R$  depend on temperature and pressure in order for calculation to match experiment reasonably. See Tawa, *et al.*, *J. Am. Chem. Soc.* 1995, 117, 1625-1628.

# application to deprotonation of monosilicic acid (i)



# deprotonation of monosilicic acid (ii)

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- \* For this equilibrium there is no loss of chemical bonds upon reaction.
- \* Reactants and products were assigned a detailed and realistic isolated molecule geometries and partial charges based upon electronic structure results.
- \* Reactants and products were assigned 'internal dielectric constants' based upon the calculated polarizabilities.
- \* The experimental free energy of deprotonation in water at T=298K is  $\Delta G^{(0)} = 13.5$  kcal/mol.

# deprotonation of monosilicic acid (iii)

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- \* **three calculations with different parameters are presented to show the importance of the parameters.**
  - » (a) no 'polarizabilities'  $\epsilon_m=1$ ; spheres on *silicon* ( $R_{Si}=1.8\text{\AA}$ ) and *oxygen* atoms ( $R_O=1.65\text{\AA}$ ), only. The oxygen radius was estimated from the calibration study.
    - ◇  $\Delta G^{(0)}=38.3$  kcal/mol (calculated).
  - » (b) same as (a) *except* :  $R_O=1.60\text{\AA}$  and  $\epsilon_m=2.95$  (acid molecule) and  $\epsilon_m=3.40$  (anion) to match molecular polarizabilities.
    - ◇  $\Delta G^{(0)}=30.0$  kcal/mol (calculated).
  - » (c) same as (b) *except* : spheres on all atoms including H ( $R_H=1.3\text{\AA}$ ,  $R_O=1.4\text{\AA}$ ,  $R_{Si}=1.8\text{\AA}$ ),  $\epsilon_m=3.10$  (acid molecule) and  $\epsilon_m=3.55$  (anion) to match molecular polarizabilities.
    - ◇  $\Delta G^{(0)}=19.8$  kcal/mol (calculated).

# deprotonation of monosilicic acid (iv)

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- \* A systematic search for radii parameters was not performed; with only one data point (the reaction free energy) those parameters are underdetermined.
- \* With the observed monotonic improvement of the model results, we felt that the experimental value could be matched with reasonable values for radii parameters.
- \* Molecular polarizabilities appear to be important for quantitative description of these reaction free energies.

# deprotonation of monosilicic acid (v)

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- \* The calibration strategy was not particularly helpful. For this case a very specific empirical calibration would probably be required to predict the reaction free energy closer than the (approximately) 30% accomplished.
- \* Spheres on acid H atoms are important for quantitative description of acid-base reaction free energies in water.



# theoretical suggestions from such studies

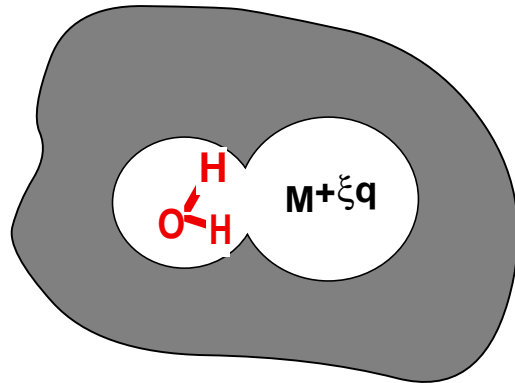
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- \* From this study and other recent studies [Hummer, *et al. J. Phys. Chem.* 1995, 99, 14188-14194] it appears that electrostatic H-bonding interactions are difficult cases for the dielectric continuum models. This may be due to the good exposure to solvent of H atoms participating in H-bonds.
- \* It is likely that these difficulties can be significantly alleviated by inclusion of neighboring H-bonded water molecules in the solute complex.

# next: a probe water molecule (i)

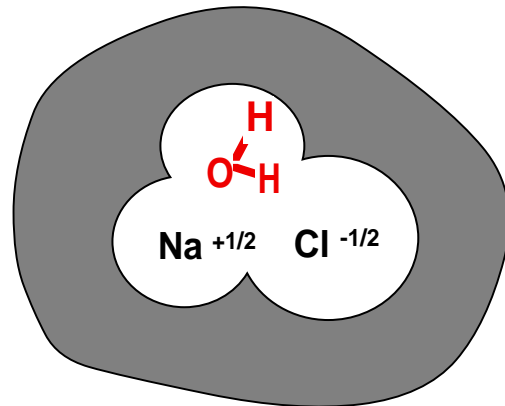
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$$\Delta\mu = \Delta\mu_0 + \int_0^q \langle \Phi \rangle_{q'} dq'$$



$$\Delta\mu = \Delta\mu_0 + q \langle \Phi \rangle_{\xi q}$$

$$\underline{\underline{\Delta\mu \approx \Delta\mu_0 + q \langle \Phi \rangle_{q/2}}}$$



## probe water molecule (ii)

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- \* **This probe water molecule approach can be used even where the structure of the first solvation shell is not physically well-defined. The model must then be used to average over shell structures.**
- \* **The probe water molecule can be incorporated also in the electronic structure calculations to treat effects such as charge transfer that are not a natural part of the existing dielectric models.**